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EXAMINER

HANLEY, SUSAN MARIE

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/589,996	<b>Applicant(s)</b> KREUTZER ET AL.	
	<b>Examiner</b> SUSAN HANLEY	<b>Art Unit</b> 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 May 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-13 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) 9, 19 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-8, 10-13, 17 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Response to Amendment***

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

### ***Claim Amendments***

The response and amendment filed 5/26/10 are acknowledged. It is noted that claim 1 is identified as "Currently Amended" but has no underlining to indicate the new text. However, the amendment has been reviewed by the examiner and approved for entry. The new text is that the ceramic honeycomb is an acicular ceramic having an aspect ratio of at least 2 in claim 1.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Election/Restrictions***

Applicant's election without traverse of the specie of claim 8, wherein the catalyst is an enzyme, in the reply filed on 06/01/2009 is again acknowledged. The restriction requirement for the specie wherein the catalyst is carbon is withdrawn since an enzyme is comprised of carbon. The specie election for claim 19 stands since a carbon fiber has a different structure (fiber) than an enzyme (three dimensional catalyst comprised of at least carbon, hydrogen and nitrogen). The specie of claim 20 stands withdrawn since the search for a carbon fiber and an enzyme are non-overlapping due to their widely different structures. The specie election for a metal stands withdrawn since a metal is a non-organic substance compared to the other organic species. Therefore, Claims 9, 19 and 20 stand withdrawn.

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Claims 1, 3-8, 10-12, 17 and 18 are under examination.

The indicated allowability of claim 15, now incorporated into claim 1, is withdrawn in view of the disclosure by Shiraishi. The English translation of JP 6-213409 (Asai et al.) is also applied.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is directed to a method for forming a reaction product by flowing a reactant into a ceramic honeycomb having an inlet and outlet that are connected by adjacent channels having thin porous walls such that the liquid substantially penetrates the into the walls and the reactant reacts as the liquid containing the reactant flows from the inlet to the outlet of the monolithic ceramic honeycomb and recovering the product from the outlet end of the ceramic honeycomb. The porosity of the partition walls is at least 50% and the mean pore size is at least 5 micrometers. The ceramic honeycomb is acicular ceramic having an aspect ratio of at least about 2. Claim 8 is directed to the elected specie, an enzyme. Claim 18 is directed to a catalyst comprising carbon. Claims 12 and 13 are directed to using a solvent that is water. Claims 3-7 recite that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

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Claims 1, 3-8, 12, 13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi (Sho58-150322; cited in the IDS filed 01/22/2007) in view of Shiraishi et al. (Hei 5-273119; cited in the IDS filed 1/22/07; translation; “Shiraishi”) and Asai et al. (English translation of JP 62134089; “Asai”; new reference).

Kobayashi teaches that microorganisms which contain enzymes (page 3, third full paragraph; claims 8 and 18) are attached to ceramic honeycomb structure via a polysaccharide (claim 1, line 6 regarding the attachment of the enzymes (microorganisms) to the ceramic structure). The ceramic honeycomb structure is advantageous because the surface is optimal for fixing microorganisms thus guaranteeing a large contact surface area with minimal pressure loss (page 3, 4<sup>th</sup> full paragraph). The fixed microorganisms have a high mechanical strength and can be used continuously for a long time (page 4, third full paragraph). Kobayashi teaches that the walls of the honeycomb are perforated with holes on the ceramic honeycomb structure to avoid the problem of obstruction and to increase contact surface area (page 3, end of the fourth full paragraph; instant claim 1, lines 5-6 regarding the porous partition walls and the flow of the reactant). The wall surface of the ceramic honeycombed structured body has multiple parallel holes (meeting the limitation of channels of a plurality of porous partition walls (claim 1).

An aqueous glucose (the reactant) solution (claims 12 and 13 directed to a water solvent) was introduced from the bottom of a reactor containing the immobilized microorganisms thus meeting the limitation of an inlet. Fermentation was accomplished using yeast and the ethanol generated from the fermentation was measured at the reactor outlet and compared (meeting the limitation of an outlet; Example 3). Thus, the ethanol was recovered as in limitation 1(b).

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Kobayashi does not teach that ceramic honeycomb is an acicular ceramic such as acicular mullite having an aspect ratio of at least about 2, wherein partition walls have a porosity of at least 50% and the mean pore size of at least 5 micrometers. Nor does Kobayashi teach that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

Asai discloses a method for making a product from a reactant wherein the reactant in a liquid flow is dispersed through a ceramic honeycomb structure having numerous pores and pluralities of through-holes (Example 3, line 21 to page 14, line 2). Microorganisms (which contain enzymes) are immobilized on honeycomb (Claim 1 on p. 2 of the translation). The average pore size of the partition wall of the ceramic honeycomb is 10 to 100  $\mu\text{M}$  (p. 2, claim 2 of the translation). The disclosure of 10  $\mu\text{M}$  and 100  $\mu\text{M}$  for the pore sizes are species that anticipate the claimed range. The values between 10 and 100  $\mu\text{M}$  are species within the prior art which suggest the same values as claimed. In example 3 (p. 13 of the translation, line 14), Asai teaches that the average pore size of the ceramic honeycomb reactor was 50  $\mu\text{M}$ , thus anticipating the claimed range of at least 5  $\mu\text{M}$ . The porosity of the honeycomb structure is 30-70% (p. 2 of the translation, claim 3). The disclosure of 70%, the upper end of the disclosed range, is a species that anticipates the claimed range. The disclosure motivates the claimed value of at least 50%. The values between 50% and 70% are species within the prior art which suggest

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the same values as claimed. In example 3, Asai discloses that the porosity of the bioreactor is 50% (line 13, page 13 of the translation), a specie that anticipates the claimed range of at least 50%. Asai teaches that the advantage of using a bioreactor having the disclosed elements is that the microorganisms/enzymes lose less activity during the immobilization process of the microorganism and provides for a large contact area between the microorganism and the substrate (p. 5, lines 18-25). Asai also teaches that the reactor can be made from mullite (p. 7 of the translation, line 6).

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to make the pore size and the porosity of the partition walls of the ceramic honeycomb reactor disclosed by Kobayashi at least 10-100 micrometers and at least 50%-70%, respectively. The ordinary artisan would have been motivated to do so because Asai teaches that ceramic honeycombed reactors having said pore size and porosity ranges have the advantage of causing less loss of activity during the immobilization process and provide for a large contact area between the microorganism and the substrate. The ordinary artisan would have had a reasonable expectation that said average pore size and porosity ranges and would be successful in the method of the Kobayashi because the reactor taught by Asai has the same set up as that of Kobayashi: a ceramic honeycomb reactor having pores with microorganisms immobilized thereon.

Shiraishi teaches that mullite is suitable for the attachment of enzymes or microorganisms or enzymes for such a carrier. Chitosan film (a polysaccharide) is easily bonded to the ceramic carrier with strong adhesion in order to support the microorganism or enzyme (page 2 of the translation, under the heading "Constitution"). The mullite is an a turf-like state that is grown

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from needle (acicular) crystals in a highly dense state (page 2 of the translation under claim 2).

The resulting ceramic carrier can support a thin film which is outstanding for the permeability of liquids (page 4, paragraph [0004]. Glucoamylase was successfully attached to said acicular mullite covered with chitosan. The fixed enzyme converted starch into glucose (Example 3, page 5 of the translation). The acicular mullite crystals are 1-100  $\mu\text{m}$  long and 0.1 to 10  $\mu\text{m}$  thick (page 2, Constitution and claim 2). The aspect ratio (length divided by thickness (width)) of the end points is 1/0.1 and 100/10 which are both a ratio of 10:1. This is a specie that anticipates the claimed range. The ratio of the lowest length value to the highest width value is 1/10 or 0.1/1. The ratio of the highest length value to the lowest width value is 100/0.1 or 1000/1. This provides an aspect ratio range of 0.1/1 to 1000/1. The ratio value of 1000/1 is a specie that anticipates the claimed range. The generic disclosure suggests or motivates the specific value, an aspect ration of 2, which is the lower end of the claimed range. The values between 2 and 1000/1 are species within the prior art which suggest the same values as claimed.

It would have been obvious to one of ordinary skill in the art, a biochemist, to make the honeycomb ceramic of Kobayashi out of acicular mullite having an aspect ratio of at 10/1 or 2 to 1000/1. The ordinary artisan would have known from Shiraishi that microorganisms, like enzymes can be fixed onto ceramics via a polysaccharide. The ordinary artisan would have been motivated to make the honeycomb ceramic monolith of Kobayashi out of acicular mullite having said aspect ratio because the adhesion of microorganisms via a polysaccharide to the acicular mullite provides a dense surface that supports the microorganisms which is outstanding for the permeability of liquids. The ordinary artisan would have had a reasonable expectation that the microorganisms would be active when attached to acicular mullite having said aspect ratio



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because Shiraishi teaches that fixed glucoamylase was able to convert starch into glucose and Kobayashi teaches that microorganisms attached to ceramics are active.

Regarding the limitations of claims 3-7, said limitations naturally flow from the factors of pore size and porosity of the monolithic ceramic honeycombed reactor since said factors govern the flow of a liquid through a honeycomb structure. In this case, the burden is shifted to Applicant to distinguish the claimed invention from the cited prior art. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claims 1, 3-8, 10-13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi (Sho58-150322; cited in the IDS filed 01/22/2007) in view of Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation) and Asai et al. (English translation of JP 62134089; "Asai"; new reference), as applied to claims 1, 3-8, 12, 13, 17 and 18, in further view of van den Broecke et al. (WO 02/33048).

The combined disclosures by Kobayashi, Shiraishi and Asai are discussed supra.

The combined disclosures do not teach that one of the reactants is a gas that is bubbled concurrently with the liquid.

van den Broecke teaches that fermentation processes involve the culturing of microorganisms, including yeast, and require a supply of oxygen for the aerobic metabolism of

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said microorganisms. Hence, oxygen is a reactant since the microorganisms require it for the fermentation process (instant claim 10). Usually the oxygen is supplied by passing an oxygen-containing gas such as air, through the liquid in the fermentation vessel. The oxygen is transferred from the gas bubbles (instant claim 11) to the liquid phase thus allowing its uptake by the microorganism (page 1, lines 6-14).

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to supply oxygen in the form of air to the microorganism in the enzyme bioreactor of the combined references by bubbling it into said bioreactor. The ordinary artisan would have been motivated to do so in order to optimize the reaction between the glucose and the immobilized microorganism. The ordinary artisan would have realized that oxygen is essential for the metabolic fermentation by the circulating yeast in order to produce ethanol. The ordinary artisan would have had a reasonable expectation that bubbling air through the reactor of the combined references would aid in the fermentation and subsequent reaction of the products of the fermentation by the immobilized microorganism because microorganisms are known to have an obligate requirement for oxygen for the fermentation process.

Claims 1, 3-8, 12, 13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncombe et al (US 4,430,348) in view of Asai et al. (English translation of JP 62134089; "Asai"; new reference) and Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation).

The content of the claims is discussed supra.

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Duncombe discloses a method for the production of a super-attenuated low calorie beer that is produced by fermenting beer though glucoamylase immobilized on a ceramic monolith. The glucoamylase is immobilized on the carrier via covalent bonds (abstract of the patent; instant claim 8, the specie for the catalyst is an enzyme; it is disposed on the ceramic surface as in instant claim 1). The limit dextrins (the reactants) are hydrolyzed by the immobilized glucoamylase by passing the beer through said monolith which is porous (see figure 2; lines 7 of instant claim 1) such that the limit dextrins come into contact with said glucoamylases that are immobilized on the ceramic surface (claim 1 of the patent). The reactor consists of a ceramic monolith having a number of discrete openings or cells within an external core. For enzyme immobilization, the maximum surface area (large number of small cells per unit cross-section ) is desired so that the maximum amount of enzyme can be attached and the reactor size can be minimized (col. 5, lines 25-36).

The reactor consists of an enzyme reactor tank having a cylindrical main body in which the ceramic monolith is disposed. The tank has a inlet at the bottom and an outlet at the top (hence it is a flow through apparatus, as required by instant claim 1). The enzyme reactor is positioned next to and is in liquid communication with a fermentation tank (col. 7, lines 30-65). In use, the fermenting beer which contains suspended yeast cells is pumped from the fermentation tank into the enzyme reactor and back to the fermentation tank. Hence, the fermentation tank receives the products of the enzyme reactor and therefore said products are recovered from the reactor tank that contains the immobilized enzyme, as in instant claim 1, part (b). The liquid is beer which contains water as in instant cams 12 and 13.

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Duncombe does not teach that the structure of the cells is a honeycomb, that the ceramic honeycomb is an acicular ceramic such as acicular mullite having an aspect ratio of at least about 2, wherein partition walls have a porosity of at least 50% and the mean pore size of at least 5 micrometers. Nor does Duncombe teach that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

The disclosures by Asai and Shiraishi are discussed supra. Shiraishi also discloses that there are a number of ways to fix enzymes and microorganisms onto bioreactors including covalent bonding. Covalent bonding has the problem that the microorganism is markedly modified or degraded by the fixation process, thus leading to a decline in the activity for the reaction. Another problem of covalent bonding is that the amount of enzyme that can be fixed is limited (page 3 of the translation paragraph [0003]).

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to use a honeycomb ceramic in the method of Duncombe. The ordinary artisan would have been motivated to do so because the honeycomb structure optimizes the surface area thus guaranteeing a large contact area and the pore size and porosity range allows for less loss of activity during the immobilization process of the microorganism. The use of the honeycomb structure would naturally allow for the penetration of the liquid containing the

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reactant, limit dextrin, to flow from the inlet to the outlet, thus, undergoing reaction (instant claim1, regarding the penetration of the liquid into the walls of the honeycomb). The ordinary artisan would have had a reasonable expectation that enzymes immobilized on a honeycomb ceramic monolith would successfully carry of the desired glucoamylase reaction because Asai demonstrates that microorganisms which are immobilized in this manner have the desired activities (Example 3). The ordinary artisan would have known from the combined references that microorganisms and enzymes can both be immobilized on ceramic surfaces for the purpose of catalyzing biochemical reactions.

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to made to make the pore size and the porosity of the partition walls of the ceramic honeycomb reactor disclosed by the combination of Asai and Duncombe at least 10-100 micrometers and at least 50%-70%, respectively. The ordinary artisan would have been motivated to do so because Asai teaches that ceramic honeycomb reactors having said pore size and porosity ranges have the advantage of causing less loss of activity during the immobilization process and providing for large contact area between the microorganism and the substrate. The ordinary artisan would have had a reasonable expectation that said average pore size and porosity ranges an would be successful in the combined method of the Duncombe and Asai because the reactor taught by Asai has the same set up as that of the combined references: a ceramic honeycomb reactor having pores with microorganisms immobilized thereon.

It would have been obvious to one of ordinary skill in the art, a biochemist, to make the honeycomb ceramic of the combined references of Asai and Duncombe out of acicular mullite having an aspect ratio of 10/1 or 2 to 1000/1. The ordinary artisan would have known from

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Shiraishi that microorganisms, like enzymes can be fixed onto ceramics via a polysaccharide.

The ordinary artisan would have been motivated to adhere the enzymes of the combined references to a honeycomb reactor comprising mullite having said aspect ratio because the adhesion of microorganisms via a polysaccharide to the acicular mullite provides a dense surface that supports the microorganisms which is outstanding for the permeability of liquids. The ordinary artisan would have had a reasonable expectation that the microorganisms would be active when attached to acicular mullite having said aspect ratio because Shiraishi teaches that fixed glucoamylase was able to convert starch into glucose (Ex. 3) Kobayashi teaches that microorganisms attached to ceramics are active.

Regarding the limitations of claims 3-7, said limitations naturally flow from the factors of pore size and porosity of the monolithic ceramic honeycombed reactor since said factors govern the flow of a liquid through a honeycomb structure. In this case, the burden is shifted to Applicant to distinguish the claimed invention from the cited prior art. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claims 1, 3-8, 12, 13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncombe et al (US 4,430,348) in view of Asai et al. (English translation of JP 62134089; "Asai"; new reference) and Shiraishi (Hei 5-273119; cited in the IDS filed

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1/22/07; translation), as applied to claims 1, 3-8, 12, 13, 17 and 18 above, and further in view of van den Broecke et al. (WO 02/33048).

The combined disclosures by the combination of Duncombe, Asai and Shiraishi are discussed supra.

The combined disclosures do not teach that one of the reactants is a gas that is bubbled concurrently with the liquid.

van den Broecke teaches that fermentation processes involve the culturing of microorganisms, including yeast, and require a supply of oxygen for the aerobic metabolism of said microorganisms. Hence, oxygen is a reactant since the microorganisms require it for the fermentation process (instant claim 10). Usually the oxygen is supplied by passing an oxygen-containing gas such as air, through the liquid in the fermentation vessel. The oxygen is transferred from the gas bubbles (instant claim 11) to the liquid phase thus allowing its uptake by the microorganism (page 1, lines 6-14).

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to supply oxygen in the form of air to the yeast in the enzyme bioreactor of the combined references by bubbling it into said bioreactor. The ordinary artisan would have been motivated to do so in order to optimize the reaction between the limit dextrose, circulating yeast and the immobilized glucoamylase. The ordinary artisan would have realized that oxygen is essential for the metabolic fermentation by the circulating yeast in order to produce the limit dextran. The ordinary artisan would have had a reasonable expectation that bubbling air through the enzyme reactor of the combined references would aid in the fermentation and subsequent reaction of the products of the fermentation by the immobilized glucoamylase because

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microorganisms are known to have an obligate requirement for oxygen for the fermentation process.

Claims 1, 3-8, 10-13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asai et al. (English translation of JP 62134089; "Asai"; new reference) in view of Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation).

Asai discloses a method for making a product from a reactant wherein the reactant in a liquid flow is dispersed through a ceramic honeycomb structure having numerous pores and pluralities of through-holes (Example 3, line 21 to page 14, line 2; meeting the limitation in claim 1 of a plurality of channels defined by a plurality of interlaced porous partition walls). In Example 3, *Acetobacter aceti* (having enzymes as in instant claims 8 and 18) was suspended in a precultivation media with a cordierite ceramic honeycomb structure having a porosity of 50% and an average pore size of 50  $\mu\text{m}$ . These are species that anticipate the claimed ranges of a porosity of 50% and at least a pore size of 5  $\mu\text{m}$ , respectively in instant claim 1. At page 14, last paragraph, Asai teaches that the process absorbs the bacteria onto the surface of the ceramic honeycomb structure, meeting the limitation of having a catalyst disposed thereon in instant claim 1). The obtained bioreactor element was place in a reactor tube. The pre-cultivation solution (instant claims 12 and 13) was introduced from the bottom of the reactor with air at the same time (instant claims 10 and 11; microorganisms need the oxygen in air to survive). The concentration of the acetic acid was measured at the reactor exit (instant claim 1, part (b)). Hence, the liquid flows from an entrance to an exit, as in instant claim 1 (a). Asai teaches that the



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method using the ceramic honeycomb structure produced a higher concentration of product compared to bacteria that was inclusion-immobilized in a bead using sodium alginate.

Asai also teaches that the average pore size of the partition wall of the ceramic honeycomb is 10 to 100  $\mu\text{M}$  (p. 2, claim 2 of the translation). The disclosure of 10 and 100 micrometers for the pore size are species that anticipate the claimed range. The values between 10 and 100  $\mu\text{M}$  are species within the prior art which suggest the same values as claimed. The porosity of the honeycomb structure is 30-70% (p. 2 of the translation, claim 3). The disclosure of 70%, the upper end of the disclosed range, is a species that anticipates the claimed range. The disclosure motivates the claimed value of at least 50%. The values between 50% and 70% are species within the prior art which suggest the same values as claimed. Asai also teaches that the reactor can be made from mullite (p. 7 of the translation, line 6).

Asai does not teach that ceramic honeycomb is an acicular ceramic such as acicular mullite having an aspect ratio of at least about 2. Nor does Asai teach that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

The disclosure by Shiraishi is discussed supra. Shiraishi also discloses that physical absorption of enzymes to a reactor has drawbacks because the enzyme was apt to peel from the carrier during the reaction because of weak adhesion between the carrier and the enzyme.

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It would have been obvious to one of ordinary skill in the art, a biochemist, to employ a ceramic honeycomb of acicular mullite having an aspect ratio of 10/1 or 2 to 1000/1, wherein the microorganisms are adhered to the mullite by a polysaccharide in the method of Asai. The ordinary artisan would have known from Shiraishi that microorganisms, like enzymes can be fixed onto ceramics via a polysaccharide. The ordinary artisan would have been motivated to adhere the microorganisms of Asai a honeycomb reactor comprising mullite having said aspect ratio because the adhesion of microorganisms via a polysaccharide to the acicular mullite provides a dense surface that supports the microorganisms which is outstanding for the permeability of liquids. The ordinary artisan would have had a reasonable expectation that the microorganisms would be active when attached to acicular mullite having said aspect ratio because Shiraishi teaches that fixed glucoamylase was able to convert starch into glucose and Asai teaches that microorganisms attached to ceramics are active.

Regarding the limitations of claims 3-7, said limitations naturally flow from the factors of pore size and porosity of the monolithic ceramic honeycombed reactor since said factors govern the flow of a liquid through a honeycomb structure. In this case, the burden is shifted to Applicant to distinguish the claimed invention from the cited prior art. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Susan Hanley/  
Examiner, Art Unit 1651

/Irene Marx/  
Primary Examiner  
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